CONFLICT OF INTEREST IN HUMAN RESEARCH

1. **PURPOSE:** To establish a service level policy for identifying, managing, and/or eliminating conflicts of interest in human research, including but not limited to the investigator, Institutional Review Board (IRB) members, Research & Development Committee (R&D) members, and the institution. The Portland VA Medical Center (PVAMC) identifies and manages conflicts of interest in human research to ensure that the protection of human research participants is the primary interest of those engaged in conducting and reviewing research. This policy ensures that conflicts of interest in human research will be identified, reviewed, and managed appropriately to uphold federal and institutional compliance and ethical standards of human research at the PVAMC, as well as safeguarding the integrity of PVAMC research.

2. **POLICY:** The PVAMC advocates full disclosure of all conflicts of interest in human research, non-financial and financial. All Principal and Co-Investigators conducting human research at the PVAMC or under PVAMC auspices must disclose all conflicts of interest regarding patents, licensing agreements, financial and non-financial interests they may have with a sponsor or otherwise of a proposed research project to the PVAMC and the potential research participant. IRB and R&D Committee members must also disclose any conflicts of interest they may have with a research project prior to the review and deliberation of the research project. Institutional conflict of interest is disclosed and considered during the review of a proposed research project in which an investigator is using his/her invention for which the Department of Veterans Affairs (DVA) has retained the rights to the invention. This policy applies to these individuals whether they are full-time employees, part-time employees, paid or unpaid consultants.

3. **RESPONSIBILITIES:**

   a. The **Associate Chief of Staff for Research & Development (ACOS/R&D)** is responsible for:
      (1) Developing and managing policies and procedures for identifying, reviewing, eliminating and/or managing conflicts of interest in research.
      (2) Ensuring all potentially significant financial or non-financial conflicts of interest have been either eliminated or minimized to uphold federal and institutional compliance and ethical standards of human research at the PVAMC.
      (3) Making final decisions in collaboration with the Medical Center Director and Chief of Staff (COS) regarding investigator appeals of R&D Committee decisions for identifying and managing conflicts of interest. Decisions made by the Director, COS and ACOS/R&D are final.

   b. The **Research and Development Committee (R&D) serves as the Conflict of Interest Committee and its members** are responsible for:
      (1) Determining whether or not any conflicts of interest exist between the chair or member of the R&D Committee and the research project to be reviewed, prior to review of the research project. If such conflicts of interest exist, the conflicted member will be recused from the vote on the research project, which is documented

in the meeting minutes. However, if during a convened meeting substantial discussion of an item with which an R&D Committee member has a conflict of interest results, then the conflicted member will step out of the room during the discussion and vote of the item. The conflicted member will be recused from the vote if a vote is required and it is documented in the meeting minutes.

(2) Reviewing all disclosed conflicts of interest identified by the Initial Review Questionnaire (IRQ) or identified otherwise during IRB review at a convened R&D Committee meeting at which a quorum is present.
   (a) Deliberating and voting on all recommendations for action to minimize, manage, monitor and/or eliminate all potentially significant financial or non-financial conflicts of interest, forwarded by the IRB.
   (b) Notifying the Principal Investigator, IRB, ACOS/R&D, and Research Assurance & Compliance Coordinator (RACC), of the decisions of the R&D Committee to minimize, manage, monitor and/or eliminate all potentially significant financial or non-financial conflicts of interest.

(3) Reviewing audit reports received from the RACC of research projects that the R&D Committee determined to have conflicts of interest and deliberating on any corrective action needed.

(4) Reviewing annual conflict of interest updates from investigators whose research projects the R&D Committee have determined has a conflict of interest, financial or non-financial.

(5) Managing institutional conflict of interest, when an investigator's proposed research project involves the investigator's invention for which the DVA has retained rights of the invention.

c. The **Institutional Review Board members** are responsible for:

(1) Avoiding conflicts of interest or the appearance of conflicts of interest. The IRB Chairpersons and members may find themselves in any of the following potential conflicts of interest when reviewing research:
   (a) Where an IRB Chairperson or member is listed as an investigator on the research.
   (b) Where any investigator must report to or is under the supervision of an IRB Chairperson or member.
   (c) Where an IRB Chairperson or member competes for research grants or contracts in the same or similar field as an investigator whose research is scheduled for review.
   (d) Where an IRB member is a family member of an investigator whose research is scheduled for review.

(2) Indicating on the IRB Reviewer Forms whether or not the IRB reviewer has a conflict of interest in reviewing the research project proposal as defined in 3.c.1. above or otherwise in this policy. The IRB member may not be the primary reviewer for a research project with which he/she has a conflict of interest. The conflicted IRB member is to call the IRB Coordinators immediately so that the research project may be reassigned and reviewed by an IRB member that does not have a conflict of interest with the research to be reviewed.

(3) Contributing the expertise and knowledge of each IRB reviewer's respective area to the review of the research project in protecting human research participants. Instances in which an IRB member reviews a research project proposal from his/her

respective department head is not necessarily considered a conflict of interest. The expertise and knowledge of the reviewer in the respective area of research outweighs the theoretical potential of a conflict of interest associated with being a member of the department.

(4) Determining whether or not any conflicts of interest exist between the chair or member of the IRB and the research project to be reviewed, prior to review of the research project as defined in 3.c.1. above or otherwise in this policy. VA human subject regulations at (38CFR16.107(e)), the Common Rule and FDA prohibit IRB members and chairs who have a conflict of interest from participating in the IRB's initial or continuing review of research. This includes all review events, e.g. initial and continuing review, adverse events, amendments, etc. During the convened meeting, if such conflicts of interest exist, the conflicted member will leave the room during the discussion and vote. The conflicted member may be invited into the room to answer members' questions during the review process. However, the member must again leave the room for the remainder of the discussion and vote on the research project. The member in conflict is instructed not to discuss the vote or who voted in any particular direction with any members of the IRB, but rather sees the discussion and vote in the IRB meeting minutes. The conflicted member will be recused from the vote on the research project, which is documented in the meeting minutes.

(5) Reviewing the IRQ and any changes of conflict of interest status and if applicable, the PVAMC "Conflict of Interest in Human Research Form", to identify potentially significant financial or non-financial conflicts of interest.

(6) Making recommendations to the R&D Committee regarding methods to minimize, manage, monitor and/or eliminate potentially significant financial or non-financial conflicts of interest.

(7) Documenting in the IRB meeting minutes the discussion, deliberation and final recommendations made to the R&D Committee.

(8) Reviewing annual conflict of interest updates from investigators whose research projects the R&D Committee has determined have a conflict of interest, financial or non-financial.

d. **Research Assurance and Compliance Coordinator** is responsible for:

(1) Preparing and maintaining conflict of interest records regarding research projects reviewed and deliberated on by the R&D Committee.

(2) Auditing on a continual basis, research projects that the R&D Committee has decided do involve investigators with a potentially significant financial or non-financial conflict of interest to ensure implementation and adherence to the decisions of the R&D Committee.

(3) Forwarding audit reports to the R&D Committee for review and deliberation.

(4) Requesting annual conflict of interest updates from investigators whose research projects the R&D Committee has determined have a conflict of interest, financial or non-financial. These will be submitted to the IRB and R&D Committee for review.

e. **Investigators** are responsible for:

(1) Indicating on the IRQ the sponsor of the study.

(2) Disclosing accurately, honestly, and completely all conflicts of interest, financial or non-financial, that they may have with a research project. Conflict of interest is reviewed and identified on the research project's IRQ. If a conflict of interest, financial or non-financial, develops or exists at any other time during the conduct of an active research project, it must be reported to the IRB.
(3) Adhering to and implementing decisions made by the R&D Committee regarding minimizing, managing, monitoring, auditing and/or eliminating conflicts of interest financial or non-financial with the research project.
(4) Maintaining the protection of human research participants' and the PVAMC's best interests in conducting studies in which the investigator may have a conflict of interest.
(5) Disclosing, when appropriate, on the informed consent form that the investigator has a conflict of interest in the research project that may potentially affect the design of, decisions made and/or actions taken surrounding the study.
(6) Submitting annual conflict of interest updates as requested by the Research Assurance & Compliance Coordinator.

4. **DEFINITIONS:**

a. **Financially Interested Business** means any business with financial interests that would reasonably appear to be affected by the conduct or outcome of any of this research project (including the sponsor of the research and/or the manufacturer or licensee of an investigational product or technology used in the research). This term includes businesses that compete with the sponsor or the manufacturer/licensee of an investigational product, if the covered individual actually knows that the financial interests of such a business would reasonably appear to be affected by the research. This term also includes any entity acting as the agent of a financially interested business (e.g., a contract research organization).

b. **Business (noun, e.g., a business):** Any corporation, partnership, sole proprietorship, limited liability company, limited liability partnership, firm, franchise, association, organization, holding company, joint stock company, receivership, business or real estate trust, or any other legal entity organized for profit or charitable purposes, but excluding the PVAMC, any affiliated hospital, any private medical practice, or any other entity controlled by, controlling, or under common control with the PVAMC.

c. **Business (verb, e.g., to do business):** Any patient care, research, teaching, or similar biomedical/health sciences activities; purchasing of goods and/or services for the provision of biomedical/health sciences activities; contracting or attempting to contract for the provision of goods and/or services to be used in biomedical/health sciences activities.

d. **Conflict of Interest:**
A conflict of interest exists when an individual 's financial interests or other obligations interfere, or appear to interfere, with the individual's 's obligations to act in the best interest of the human research participants and the PVAMC and without improper bias. This may include both financial and non-financial conflicts of interest. The mere appearance of a conflict may be as serious and potentially damaging to the public trust as

an actual conflict. Therefore, potential conflicts must be disclosed, evaluated, and managed with the same thoroughness as actual conflicts.
Note: Additional instances where an IRB Chairperson or member may have a conflict of interest are indicated in section 3.c.1. above.

e. **Executive Position:** Any position that includes responsibilities for a material segment of the operation or management of a business. This would include a position on a Board of Directors.

f. **Family:** A spouse and/or dependent child/children.

g. **Intellectual Property:** Intellectual property includes any invention or improvement in technology, whether patentable or not, conceived or developed using the expertise for which an employee is employed by the PVAMC, PVAMC facilities, personnel, information, or other resources; educational professional or tangible materials, whether or not registered for copyright or trademark, that result from the instructional, research, or public service activities of the PVAMC and data developed using PVAMC facilities, personnel, or other resources or resulting from the instructional, research, or public service activities of PVAMC.

h. **Investigator:** The term investigator as used in this policy means the principal investigator, co-investigator and other PVAMC employees, volunteers, or any PVAMC research collaborators, including visiting scientists, under the direction of the Principal Investigator (PI) who is involved in some or all aspects of the research project, including the: design of the study, conduct of the study, analysis and interpretation of the collected data, and writing of resulting manuscripts. "Investigator" includes the investigator's spouse and dependent children. This may also include students, post-doctoral fellows, and other staff.

i. **Non-Financial Conflict of Interest:**
This may exist when an individual serves dual roles, such as investigator and health care provider. Other interests, such as publication, promotion or tenure, can also become conflicts of interest that may affect an individual's judgment.

j. **Participate:** To be part of the described activity in any capacity or position that may influence an outcome.

k. **Project Period:** The project period should match the performance dates on the grant or contract or similar document. This may be an anticipated start and completion date.

l. **Significant Financial Interest (SFI):**
Significant financial interest includes the following interests of the investigator (and his or her spouse and dependent children) or of any business controlled or directed by the individual or his or her spouse:

(1) Equity interests, including stock options, of any amount in a non-publicly traded, financially interested business (or entitlement to the same)

(2) Equity interests (or entitlement to the same) in a publicly traded, financially interested business that exceed the defined de minimis amount (see exceptions below).

(3) Royalty income or the right to receive future royalties under a patent license or copyright, where the research is directly related to the licensed technology or work.

(4) Service as an officer, director, or in any other executive position for a financially interested business, whether or not remuneration is received for such service

(5) Any non-royalty payments or entitlements to payments in connection with the research that are not directly related to the reasonable costs of this research (as specified in the research agreement between the sponsor and the institution). **Note:** This includes any bonus or milestone payments to the investigators in excess of reasonable costs incurred, whether such payments are received from a financially interested business or from the institution.

(6) Consulting fees, honoraria (including honoraria from a third party, if the original source is a financially interested business), gifts or other "in kind" compensation from a financially interested business (or entitlement to the same), whether for consulting, lecturing, service on an advisory board, or for any other purpose not directly related to the reasonable costs of conducting this research (as specified in the research agreement), that in the aggregate have in the prior calendar year exceeded the de minimis amount established in PHS regulation (presently $10,000), or are expected to exceed that amount in the next twelve months.

The term "significant financial interest" does not include the following:

(1) Interests of any amount in publicly traded, diversified mutual funds.

(2) Stock or stock options in a publicly-traded company that (when valued in reference to current public prices or using accepted valuation methods) doesn't exceed $10,000 in value and does not represent more than 5% ownership interest in any single entity.

(3) Payments to the institution, or via the institution to the individual, that are directly related to reasonable costs incurred in the conduct of research as specified in the research agreement(s) between the sponsor and the institution.

(4) Salary or other remuneration from the PVAMC, including earnings and the distribution of those earnings that may be established by departmental or other similar agreements provided that those agreements and departmental/divisional group plans are approved by the Medical Center Director.

(5) Income from occasional seminars, lectures, or teaching engagements sponsored by public or nonprofit entities.

(6) Income from service on advisory committees or review panels for public or nonprofit entities (including scientific and technical groups) commissions, committees of professional associations related to the employee's work and consultations with persons in other governmental agencies or not for profit organizations on matters of mutual interest to the entity and the PVAMC.

5. **PROCEDURES:**

a. **Disclosure of Conflicts of Interest**

(1) **Research & Development Committee Members**

Determining whether or not any conflicts of interest exist between the chair or member of the R&D Committee and the research project to be reviewed, prior to review of the research project. If such conflicts of interest exist, the conflicted member will be recused from the vote on the research project, which is documented in the meeting minutes. However, if during a convened meeting substantial discussion of an item with which an R&D Committee member has a conflict of interest results, then the conflicted member will step out of the room during the discussion and vote of the item. The conflicted member will be recused from the vote if a vote is required and it is documented in the meeting minutes.

(2) **Institutional Review Board Members**

(a) Indicating on the IRB Reviewer Forms whether or not the IRB reviewer has a conflict of interest in reviewing the research project proposal as defined in 3.c.1. above or otherwise in this policy. The IRB member may not be the primary reviewer for a research project with which he/she has a conflict of interest. The conflicted IRB member is to call the IRB Coordinators immediately so that the research project may be reassigned and reviewed by an IRB member that does not have a conflict of interest with the research to be reviewed.

(b) Determining whether or not any conflicts of interest exist between the chair or member of the IRB and the research project to be reviewed, prior to review of the research project as defined in 3.c.1. above or otherwise in this policy. VA human subject regulations at (38CFR16.107(e)), the Common Rule and FDA prohibit IRB members and chairs that have a conflict of interest from participating in the IRB's initial or continuing review of research. This includes all review events, e.g. initial and continuing review, adverse events, amendments, etc. During the convened meeting, if such conflicts of interest exist, the conflicted member will leave the room during the discussion and vote. The conflicted member may be invited into the room to answer members' questions during the review process. However, the member must again leave the room for the remainder of the discussion and vote on the research project. The member in conflict is instructed not to discuss the vote or who voted in any particular direction with any members of the IRB, but rather sees the discussion and vote in the IRB meeting minutes. The conflicted member will be recused from the vote on the research project, which is documented in the meeting minutes.

(3) **Investigators** are required to report all sponsors of proposed research projects and conflicts of interest with the proposed research project. During the initial review of the research project this is indicated on the IRQ. At any future time, if a conflict of interest exists or changes during the conduct of an active research project the Investigator must report it to the IRB.

(4)**Informed consent forms** for research projects, which the R&D Committee determines an investigator has a significant financial or non-financial conflict of interest, must disclose this conflict of interest. The R&D Committee will concur on the language to be included in the informed consent form to inform potential research participants.

b. **Review of Research Projects with Significant Financial or Non-Financial Other Conflicts of Interest**

(1) Research projects for which an IRB or R&D Committee Chairperson or member has a significant financial or non-financial conflict of interest with a research project to be reviewed by the respective committee may not participate in the review, discussion and vote of the research project. Additionally, any conflicted member of a committee will not be assigned to be the primary reviewer of a research project for which he/she is identified as an investigator of the research.

(2) Research projects for which an investigator indicates either a positive response to the conflict of interest questions on the IRQ or at a future time during the conduct of the active research project, will be reviewed and discussed by the IRB. The IRB will discuss possible mechanisms for either minimizing, managing, monitoring and/or eliminating the conflict of interest.

(3) The IRB will document in the meeting minutes the discussion, deliberation, and final recommendations of the possible mechanisms to minimize, manage, monitor and/or eliminate the conflict of interest and forward the meeting minutes to the R&D Committee.

(4) The R&D Committee will review the Portland VA Medical Center "Conflict of Interest in Human Research Form," and the IRB minutes documenting the discussion, deliberations and recommendations of the proposed mechanisms for minimizing, managing, monitoring and/or eliminating the conflict of interest.

(5) The R&D Committee will decide and vote on all recommendations for action to minimize, manage, monitor and/or eliminate all potentially significant financial or non-financial conflicts of interest, forwarded by the IRB.

(6) The R&D Committee will notify the Principal Investigator, IRB, ACOS/R&D, and RACC, regarding the decisions of the R&D Committee to minimize, manage, monitor and/or eliminate the possible impacts of all potentially significant financial or non-financial conflicts of interest.

(7) The investigator must adhere to the decisions made by the R&D Committee, regarding the research project and the potentially significant financial or non-financial conflicts of interest.

(8) An investigator may appeal a decision made by the R&D Committee to the ACOS/R&D in writing only and must be made within ten days of first notification to the investigator. Appeals may be based only upon grounds of procedural irregularity that resulted in prejudice to the investigator, inclusion of new applicable information not available at the time of review and deliberation or if the decisions are inconsistent

with federal and state laws and/or institution policies. The Medical Center Director, COS, and ACOS/R&D will deliberate and make a final decision regarding the conflict of interest. This decision is final.

(9) The Research Service shall keep and maintain records, identifiable to each award, of all disclosures of relationships between Investigators and potential Research sponsors and all actions taken to manage any actual or potential conflicts of interests for at least six (6) years beyond the termination or completion of the award or until resolution of any action by any federal agency involving the records, whichever is longer.

(10) Implementation of continuous quality improvement, includes the annual audit of those research projects for which the R&D Committee decided has a significant financial or non-financial conflict of interest by the RACC. This will ensure the implementation of and adherence to the R&D Committee's decided mechanisms for minimizing, managing, monitoring and/or eliminating the conflict of interest.

(11) The continuous quality improvement audit reports from the RACC will be forwarded to and reviewed by the R&D Committee. If the decisions previously made by the R&D Committee have not been implemented and adhered to, corrective action will be taken.

d. **Institutional Conflict of Interest**

(1) The R&D Committee will evaluate PVAMC institutional conflict of interest for all proposed research projects in which an investigator is using his/her invention for which the DVA has retained the rights following a disclosure of invention.

(2) Investigators must disclose their inventions to the DVA. Investigators proposing research project, which will involve their own invention(s), must submit the official letter from the Office of General Counsel describing the determination of rights with the Portland VA Medical Center "Conflict of Interest in Human Research Form."

(3) When the DVA maintains the rights to an investigator's invention, which will be used in a proposed research project, the R&D Committee will seek recommendations from the Department of Veterans Affairs Regional Counsel.

(4) The R&D Committee will deliberate on the recommendations made by the Regional Counsel and make a final decision, regarding the conflict of interest in the proposed research project. A decision will be made to either eliminate or reduce and manage, as well as monitor the institution's conflict of interest confirmed by the R&D Committee.

e. **Mechanisms for Managing Significant Financial or Non-Financial Conflicts of Interest**

The IRB and DVA Regional Counsel may recommend and the R&D Committee may deliberate on mechanisms to be implemented to minimize, manage, monitor, and/or eliminate the conflict of interest. Recommendations and deliberations may include the following mechanisms:

(1) Modification of the research proposal or procedures;

(2) Monitoring of the research project by the RACC or other institutional or independent reviewer;

(3) Disclosing publicly the investigator's financial or non-financial conflict of interest in any research sponsor or the commercial success of any therapeutic strategy or product that is the subject of any research data or results being reported;
(4) Disclosing on the informed consent document the relationship and payment information of the sponsor to the investigator, the investigator's significant financial or other type of conflict of interest. Also disclosed will be the institution's mechanism for minimizing, managing, monitoring and/or eliminating the conflict of interest.
(5) Divestiture by an Investigator of any financial interest in any research sponsor;
(6) Requiring that the investigator eliminate direct engagement with the research project through any of the following: design of the research project, monitoring any aspect of the project, obtaining informed consent, adverse event reporting, or analyzing and reporting of the data;
(7) Severing any relationship between an Investigator and a research sponsor, which may create actual or potential conflicts of interest.
(8) Prohibiting the research project from being conducted at the PVAMC.
(9) Sections 3.b.1., 5.a.1., and 5.b.1. also outline preferred and allowable remedies to manage or eliminate the conflict of interest of R&D Committee members.
(10) Sections 3.c.1-4, 5.a.2., and 5.b.1 also outline preferred and allowable remedies to manage or eliminate the conflict of interest of IRB members.

6. REFERENCES: 21 CFR 312.64 (d)
21 CFR 56.107(e)
38 CFR 16.107 (e)
45 CFR 46.107 (e)
M-3, Part I, 9.08(e)

7. CONCURRENCES: Endorsed by the Research & Development Committee, 06/28/2004

8. RESCISSION: HRPP: Policy & Procedure No. 5, Conflict of Interest in Human Research endorsed by the R&D Committee 08/26/2002, 09/23/2002, 05/19/2003, and 10/27/2003

9. FOLLOW-UP RESPONSIBILITY: ACOS, Research & Development Service (R&D)

MICHAEL P. DAVEY, M.D., PH.D.
ACOS, Research & Development Service